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Gang Yao, Lihong V. Wang, "Simulation study of ultrasound-modulated optical tomography," Proc. SPIE 4256, Biomedical Optoacoustics II, (15 June 2001); doi: 10.1117/12.429307

Event: BiOS 2001 The International Symposium on Biomedical Optics, 2001, San Jose, CA, United States

Simulation Study of Ultrasound-Modulated Optical Tomography

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ABSTRACT

Monte-Carlo modeling technique was used to simulate the ultrasound-modulated optical tomography. The difference between absorption and scattering objects was compared. Simulation result indicated that this technique is sensitive to object absorption property, while the scattering properties have less effect on the output AC/DC signal intensity. It was also demonstrated that inhomogeneity and the background optical properties of the scattering medium could change the AC/DC value. The signal-to-noise ratio problem in the experiment is carefully analyzed. The major noise source is the speckle noise caused by the small particle movement within the tissue sample. The decorrelation time of the speckle pattern was measured in the tissue sample. In order to reduce the speckle noise, the data acquisition time must be less than the speckle decorrelation time.

Key words – optical imaging, ultrasound modulation, biological tissue.

1. INTRODUCTORY

A number of optical imaging techniques[1] have been studied for imaging in biological tissues. The key challenge is to overcome the strong scattering of light in biological tissues. Besides purely optical imaging techniques, techniques combining optical techniques and ultrasonic techniques have also been explored because ultrasonic waves scatter much less in biological tissues than optical waves and can directly furnish localization information for imaging. Ultrasound-modulated optical technique[2-5] is one of such hybrid methods. Marks *et al.*[2] investigated the possibility of tagging light with ultrasound. Wang *et al.*[3] developed ultrasound-modulated optical tomography and obtained images in tissue-simulating phantoms. A single-detector scheme was usually used in these early studies. Leveque *et al.*[6] developed a parallel speckle detection scheme using a source-synchronized lock-in technique, in which a CCD camera worked as a detector array. The signal-to-noise ratio (SNR) can be greatly improved by averaging the signals from all of the CCD pixels. They obtained one-dimensional (1D) images of buried object in real biological tissue (turkey breast). Yao and Wang[7] implemented this technique and successfully obtained 2D images in chicken breast tissue with two buried objects. In order to achieve spatial resolution along the ultrasonic axis, Wang and Ku[8] developed a technique called frequency-swept ultrasound-modulated optical tomography. In their experiment, one frequency-sweep function (chirp) excited the ultrasonic transducer while another chirp modulated the gain of the optical detector. When the heterodyne signal from the optical detector was Fourier transformed, the signal from a specific spatial location was converted into a specific frequency component. However, because of the limited SNR of the single-detector scheme, this technique was demonstrated only for ballistic imaging. Yao *et al.*[9] combined frequency-swept technique with source synchronized detection and successfully obtained 2D images in chicken breast tissue with buried objects. They also demonstrated the scalability of the spatial resolution along the ultrasonic axis by adjusting the parameters of the chirp function.

In this report, we studied some fundamental problems in ultrasound-modulated optical tomography. Monte-Carlo technique was used in our simulation studies because it is the most accurate tool in studying light transport in turbid media. The modulation mechanisms were not incorporated in the simulation. We simply focused on the calculation of the number of photons passing through the ultrasonic column. Although the simulated results can not

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Biomedical Optoacoustics II, Alexander A. Oraevsky, Editor,
Proceedings of SPIE Vol. 4256 (2001) © 2001 SPIE · 1605-7422/01/$15.00

be compared directly with the experimental results, the simulation study can assist in the understanding of some basic physical aspects of this imaging technique. We also studied the effects of speckle noise which is the most important noise in the experiments of biological tissue.

2. SIMULATION STUDY

In ultrasound-modulated optical tomography, the transmitted light consists of two parts: the AC photons that are modulated by the ultrasonic wave; and the DC background photons that are not modulated. The AC photons contribute to the signal and depend on two factors: the number of modulated photons and their modulation depth. The modulation depth is related to the intensity of the ultrasonic wave and the modulation mechanisms.[10,11] Only the photons passing through the ultrasonic column could be modulated. The number of modulated photons is related to the optical properties of the scattering media and the size of the modulation column that determines the spatial resolution. Therefore, the quantity AC/DC reflects the local optical and mechanical properties within the ultrasonic beam and can be used for tomographic imaging of the tissue.

Monte-Carlo method was used to simulate ultrasound-modulated optical tomograph, the transmitted light passing through the ultrasonic column is scored as the AC signal, and the other transmitted photons were scored as the DC signal. The basic simulation procedures have been described in detail elsewhere.[12] The program is extended to handle multiple objects to simulate the effect of heterogeneous background. The photon packet was launched perpendicularly into the tissue. A photon was labeled as the AC photon whenever it interacted with the ultrasonic column, either being scattered in this column or directly passing through it. Geometrical calculations were performed to decide if the photon intercepted with one of the objects and the photon scattering angles were sampled according to the specific local optical properties.

In the simulation, the tissue sample was modeled as a slab with buried objects. For simplicity, the object and ultrasonic column were modeled as cylinders. The height of the ultrasonic column was 2 cm and the radius was assumed to be 1 mm. Unless indicated specifically, the following values were used to simulate the optical properties of the chicken breast tissue:[13] the refractive index n = 1.33, the absorption coefficient $\mu_a = 0.1$ cm^{-1}, the scattering coefficient $\mu_s = 20.0$ cm^{-1}, and the anisotropy factor $g = 0.9$. A light beam with radius of 1cm incidents perpendicularly upon the turbid medium. Only the transmitted photons within a circular disk of a 1-cm radius on the exit plane were scored, which simulated the detection area.

2.1 Contrast and sensitivity

In ultrasound-modulated optical tomography, the AC photons carry the optical as well as mechanic properties of the ultrasonic column. If the optical properties within the ultrasonic column are different, the detected signal will be different. In order to study the effect of these different optical properties, we simulated objects with different absorption coefficient and scattering coefficient. The simulation results are show in Fig. 1. The thickness of the tissue slab is 3 cm. A single cylindrical object is buried at the center of the tissue slab. The position of the ultrasonic column is aligned with the object (Fig. 1d). Both the object and ultrasonic column have a radius of 1mm and a height of 6mm. Therefore, every photon passing through the object will be labeled by the ultrasound. The values in the plots are normalized to the values (AC/DC = 0.08) when the ultrasonic column is positioned at background tissue. In Fig. 1c, the x-axis is reduced scattering coefficient: $\mu_s' = \mu_s(1-g)$, and μ_s is constant (20 cm^{-1}) in the calculation.

From the simulation results, the AC/DC decreases as the absorption coefficient and the scattering coefficient of the object increases. This is because that more photons passing through the object have been absorbed or scattered. The AC/DC increases as the anisotropic factor increases because more modulated light is scattered forwardly. The AC/DC is much more sensitive to the change of optical properties than the total output intensity (AC+DC). For example, as the optical absorption coefficient increases by 100 times, the AC/DC decreases by more than 80%, while (AC+DC) only decreases by ~12%. The object scattering property (μ_s and g) has less effect on AC/DC than the object absorption property (μ_a). In the example, when the object absorption coefficient, scattering coefficient, μ_s' increase by 100 times, the AC/DC decreases by ~ 80%, 12%, and 25% respectively. Obviously, the AC/DC is much more sensitive to the change of the absorption coefficient of the object. Depending on the sensitivity of the system, it is usually easier to detect absorption objects than scattering objects.

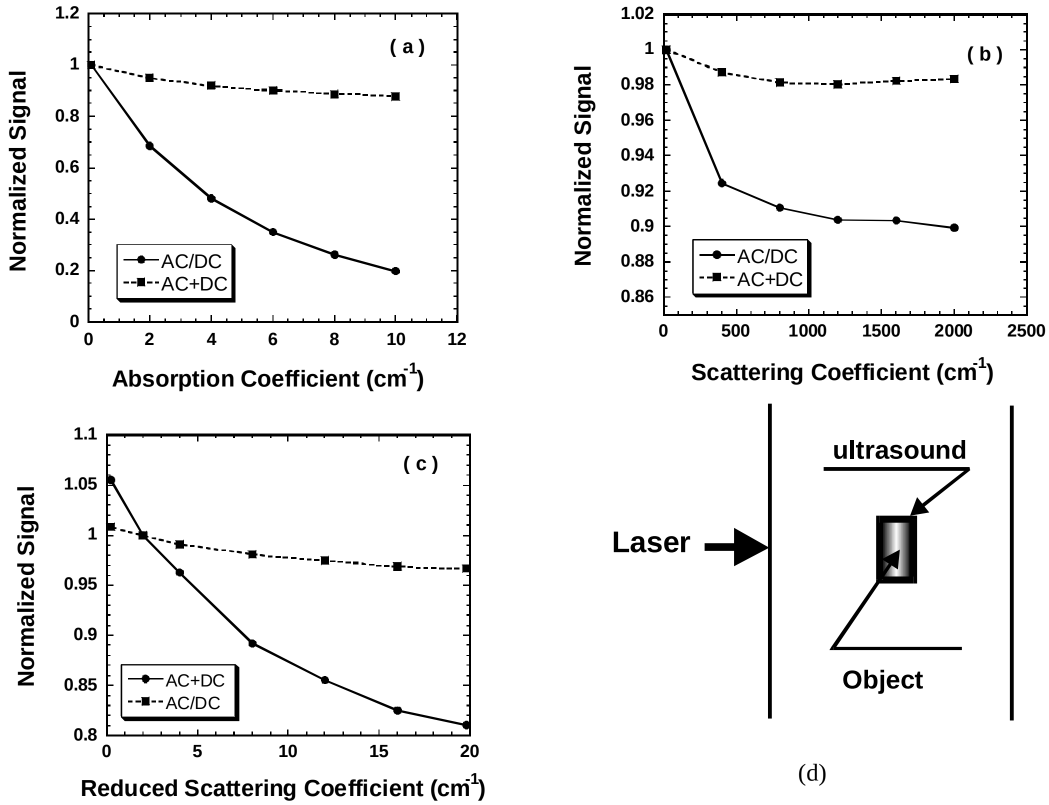

Fig. 1. AC/DC at a single object with different (a) absorption coefficient, (b) scattering coefficient, and (c) reduced scattering coefficient; (d) schematic setup.

2.2 Signal variation with scanning position

In the experiment of ultrasound-modulated tomography, two-dimensional images are usually obtained by mechanically scanning the ultrasonic transducer or the sample. As shown in the above simulations, the AC signal will depends on how many photons passing the ultrasonic column. Because the light flux distribution is not uniform within the scattering medium, we expect that the AC/DC signal be related to the position of the ultrasonic column even for a homogeneous medium.

One-dimensional scans along the *Z* axis and the *X* axis of a 1.5-cm thick chicken breast tissue were simulated. An absorbing object was buried in the middle plane of the sample. Figure 2a shows the result when the scan line was far way from the absorption object. The AC/DC signal decreases when the ultrasonic column moves away from the light source, which is caused by the internal photon distribution inside the tissue sample. The photon fluence is larger at positions near the incident light source where they have more chances to pass through the ultrasonic column. Figure 2b shows the result when the scan line passed through the center of the object. Clearly, the signal is smaller when the ultrasonic column is coincident with the object. In order to compensate the signal variation caused by the internal photon distribution, we can normalize the signal in Fig. 2b with the background signal in Fig. 2a. The normalized signal is plotted as a dashed line in Fig. 2b. Obviously, the normalized result is much smoother and has a higher contrast.

Figure 3 shows the result for the scan along the *X* axis. The diffuse transmittance (AC + DC) is also plotted as a reference. As expected, the AC/DC curve had sharper resolution and a better contrast than the diffuse-transmittance curve. Because the diameter of the ultrasonic column was ~2 mm, the object size measured from the AC/DC curve was larger than its actual size of 2 mm. The spatial resolution in ultrasound-modulated optical imaging is determined by the size of the ultrasonic column.

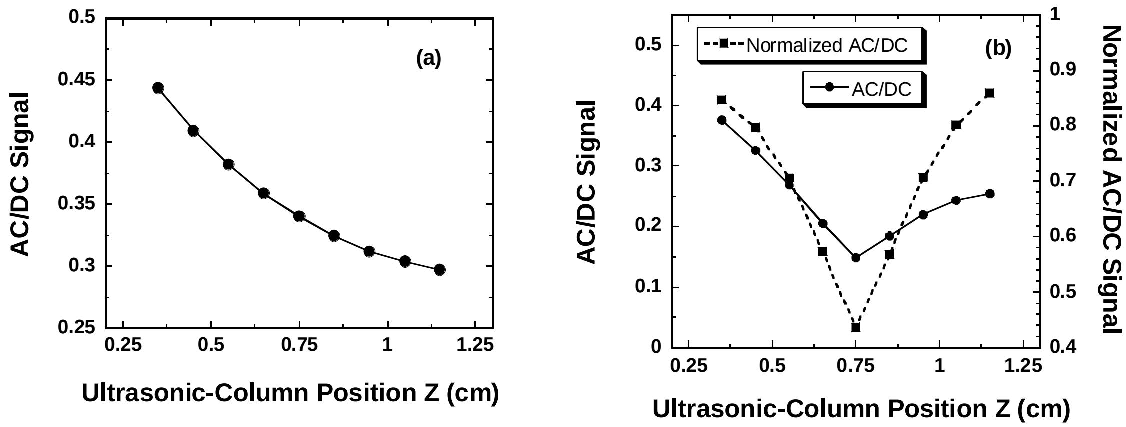

Fig. 2. Simulated 1D images along the *Z* axis (optical axis). The light was incident at *Z* = 0. (a) The AC/DC signal when the scan line was far away from the object; (b) The AC/DC signal when the scan line passed through the object.

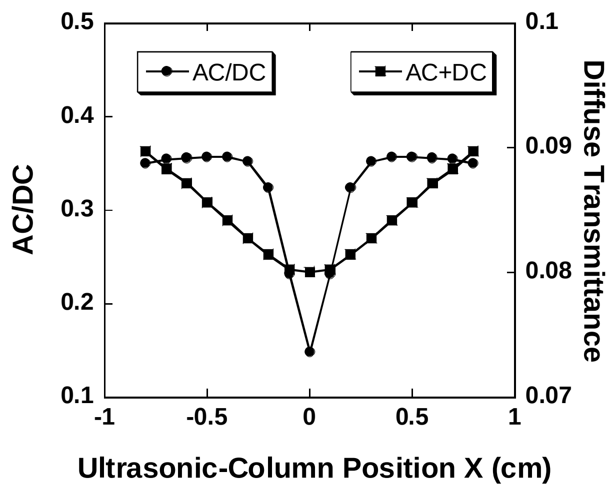

Fig. 3. Simulated 1D image along the *X* axis with the scan line passing through the center of the object.

2.3 Effect of sample inhomogeneity

In reality, tissue samples are inhomogeneous in both absorption and scattering properties. Because the local modulated signal intensity will dependent on the local optical flux, the internal optical flux will affect the obtained image. More specifically, a buried object will affect the optical flux in its neighborhood and the modulated signal intensity. Figure 4 shows an example in which two identical objects are separated by 3mm along the Z-axis. The ultrasonic column is located at Object-2 which is at the center of the slab. From the results (Fig. 5), the calculated AC/DC is affected by the optical properties of the other object. As the absorption coefficient and the scattering coefficient of Object-1 increase, the AC/DC values of Object-2 decrease because the light passing through the ultrasonic column (located at Object -2) decreases. In other words, Object-1 casts a shadow on Object-2. It must be pointed out that Object-2 is still detectable in the example. However, its signal intensity is changed with the appearance of the second object. Actually, the absolute signal level is also affected by the optical properties of the background medium.

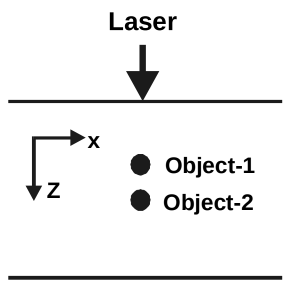

Fig. 4. Configuration of the two objects in the simulation

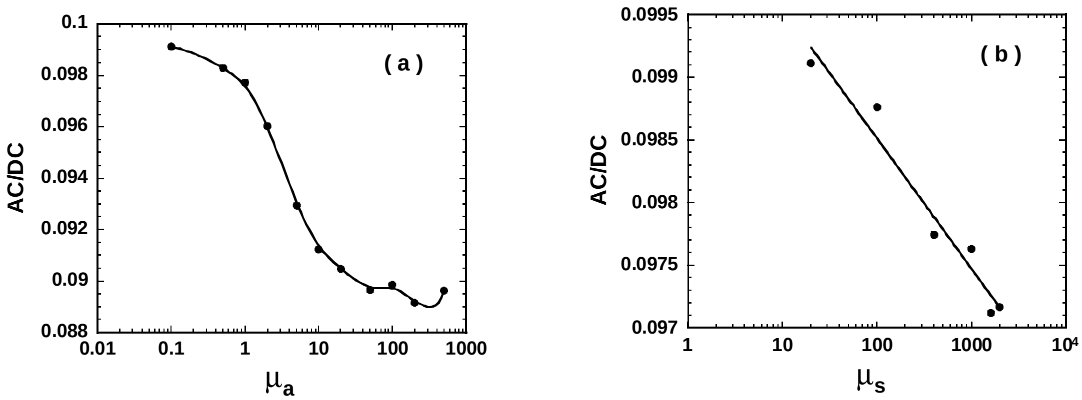

Fig. 5. The effects of neighborhood objects. Two objects are separated by 3 mm along Z-axis.

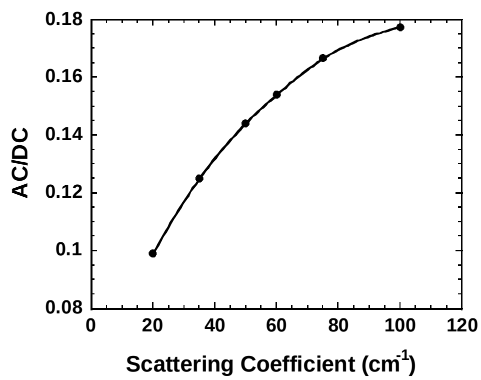

Fig. 6. AC/DC change with background scattering coefficient

In Fig. 6, the AC/DC of a single object was calculated with different background scattering coefficient. The object was positioned at the center of the turbid medium. The interesting thing is that more photons are scattering from the ultrasonic column as the background scattering coefficient increases, which causes the increase of AC/DC.

The above several examples indicate that the signal intensity is indeed related to the background properties and objects distribution in the medium. Therefore quantitative measurements of the objects' optical properties is quite difficult unless special data processing methods, such as the image reconstruction algorithm, are applied.

3. SPECKLE NOISE

In ultrasound-modulated optical tomography, the signal-to-noise ratio (SNR) is more critical because the modulated signal is very small. In order to achieve better experimental result, the system noise properties should be carefully analyzed and optimized. There are several possible noise sources in the experimental system. The first one is the thermal noise of the CCD detector. The second one is the light intensity noise induced by laser source power fluctuation. The speckle decorrelation also contributes to the noise. Shot noise is the theoretical limit of noise. The speckle noise appeared to be the most significant noise source in biological tissue. It is caused by the movement of small particles within the biological tissue. In order to demonstrate the speckle noise, the stability of the system was examined by using a ground glass as the sample without ultrasound modulation. The laser light incident upon the ground glass and the generated speckle pattern was recorded by the CCD camera (DALSA CA-D1-0256T). 200 frames of such speckle images were recorded, and the standard deviation of each pixel in the CCD image was calculated. The total acquisition time was ~ 3.2s. The calculated standard deviation for each pixel was normalized to the shot noise obtained by square root of the average pixel count. As shown in Fig. 7a, the measured noise level was within two times of shot noise when ground glass was used and the light path was in the air. So it is demonstrated that the whole experimental system was almost working at the shot noise limited level.

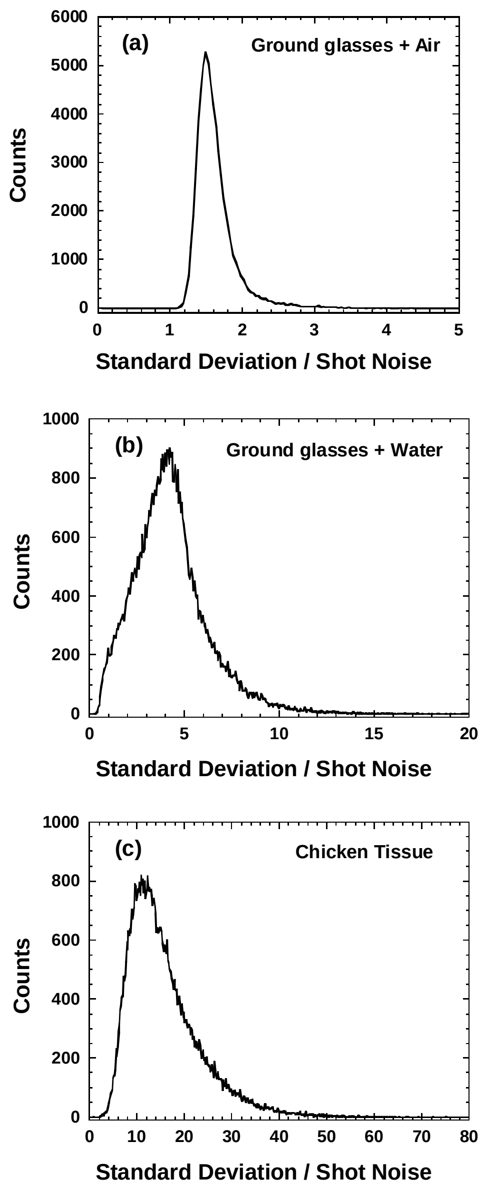

Fig. 7. Speckle pattern stability at different sample configurations.

However, the noise level increased to more than 5 times of shot noise when a water tank was inserted into the light path between the ground glass and the CCD (Fig. 7b). This was caused by the fluctuation of water or the movement of some small particles within the water, which disturbed the speckle pattern. The noise level further increased to more than 10 times of shot noise when a chicken breast tissue was used instead of the ground glass. One reason is that chicken breast tissue is volume scattering medium, where light has longer pathlength. The movements of small particles within the tissue disturb the speckle patterns. It is clear that this dynamic speckle change is the major noise source in the experiments. Increasing the exposure time could reduce the speckle fluctuation. Unfortunately, this effect is equivalent to speckle average and it reduces the modulation depth. The correct way is to acquire the signal within the speckle correlation time. The correlation time can be measured in the experiments by continuously acquiring multiple frames of images. In the experiments, the four sequential frames need to be acquired within the speckle correlation time, which is about several hundreds of milliseconds for *ex vivo* chicken breast tissue (Fig. 8).

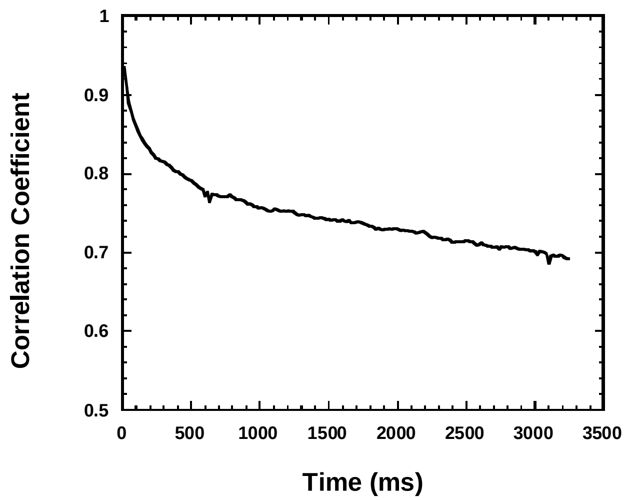

Fig. 8. Speckle correlation time measured from 1.2 cm thick chicken breast.

Because modulated AC light (I_{AC}) and un-modulated DC light (I_{DC}) have different pathlength distributions, they generate two different speckle patterns. Therefore, the modulation depth (I_{AC} / I_{DC}) is not uniform. If a single detector were used to detect a single coherent area (a speckle), the output signal would be position dependent. The phase φ of the modulated signal is also spatially randomized. The variations of φ have different properties at two different spatial scales. Within a single speckle, the change of the phase is slow; while the phases are statistically randomized between different speckles. This phenomenon implicates that the signal intensity strongly depends on the number of speckles within the detection area. Statistically, the DC component I_{DC} increases linearly with the number of speckles, while the AC component I_{AC} increase with the square root of number speckles. Consequently, the modulation depth (I_{AC} / I_{DC}) decreases with the square root of the number of speckles. In other words, averaging over multiple speckles will decrease the modulation depth because the signal phase is randomized for a speckle field. This is an important result that plays critical role in speckle related experiments.

4. CONCLUSION

The ultrasound-modulated optical tomography has the potential for early detection of breast cancers, because it combines the contrast advantage of purely optical imaging and the resolution advantage of purely ultrasonic imaging and optical properties are related to tissue constituents and their molecular conformations. The unique property of ultrasound-modulated optical tomography is that it can achieve high spatial resolution and maintain the optical contrast at the same time. The spatial resolution mainly depends on the focal spot size of the ultrasonic transducer, which is related to the ultrasonic frequency and its geometrical parameters. For a 1MHz transducer, the typical spatial resolution is 1 mm. If the frequency is 100 MHz, 10 μm resolution can be achieved. In addition, both modulation mechanisms predict that the modulation depth increase with the ultrasonic frequency. This implicates that the signal-to-noise ratio could be improved at higher frequency range. On the other hand, the penetration depth of the ultrasonic wave decreases as the ultrasonic frequency increases.

According to the ultrasonic frequency, there are two potential application categories for ultrasound-modulated optical tomography. In t he first category, we can use high frequency ultrasound (hundreds of megahertz) to achieve high spatial resolution (~10 μm) with several millimeter penetration depth. This would be very useful diagnosis of surface lesions including skin cancer and GI tract problems. In the second category, low frequency ultrasound (several megahertz) can be used to achieve millimeter spatial resolution with several centimeter penetration depths. This can be used in early breast cancer detection.

The optical speckle played an extremely important role in the experiments. Single speckle detection is necessary to maintain high modulation depth. Due to the spatial variation of the signal, multiple measurements over the speckle field are mandatory to achieve a stable value for imaging purpose. Furthermore, the speckle patterns are changing with time in laser-tissue interaction. As mentioned before, this is the largest noise in the experiment, especially with thick biological tissue. To lessen this problem, the data needs to be acquired within the speckle correlation time.

ACKNOWLEDGMENT

This project was sponsored in part by National Institutes of Health grants R29 CA68562, R01 CA71980, and R21 CA83760, National Science Foundation grant BES-9734491, and Texas Higher Education Coordinating Board grant 000512-0123-1999.

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